GP 1804
4/10 attach
T.D.P

8/410,539
Exr Campbell
AU 1819

RECEIVED
JUN 14 1996
GROUP 1800

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner of Patents and Trademarks, Washington, D.C. 20231, on May 31, 1996
Date of Deposit

Alice O. Martin
Name of applicant, assignee or Registered Representative

Signature

May 31, 1996
Date of Signature

MAIL ROOM JUN 4 1996 10 PAT. & TRADEMARK OFF.

Case No. 7823/5

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	
Matthew B. Wheeler	Group Art No.:
Serial No.: 08/410,539	Examiner:
Filed: March 24, 1995	
For: TRANSGENIC UNGULATE METHODS AND COMPOSITIONS	

INFORMATION DISCLOSURE STATEMENT

Assistant Commissioner of
Patents
Washington, D.C. 20231

Dear Sir:

Pursuant to the obligation under 37 C.F.R. § 1.56 and in conformance with 37 C.F.R. §§ 1.97-1.98, Applicant hereby submits the following list of references for consideration by the Examiner. Pursuant to 37 C.F.R. §1.98(d), copies of some of these references are not being provided since they were cited by or submitted to the U.S.P.T.O. in the parent case. Included in the present submission is the International Search Report for a related case. Included in the present submission is the International Search Report for a related case, in particular, the present application is a continuing application of U.S. Ser. No. 08/063,095, filed May 14, 1993, and to be issued as U.S. Pat. No. 5,523,226. If the Examiner would like copies of any of the references listed, please contact the undersigned attorney.

U.S. Patents

Patent No.	Issue Date	Inventor	Filing Date
5,175,383	12/1992	Leder *et al.*	02/17/89
5,175,384	12/1992	Krimpenfort *et al.*	12/05/88
5,175,385	12/1992	Wagner *et al.*	09/03/87

Foreign Patent Documents

DOCUMENT NUMBER	DATE	COUNTRY
EP 0169672	01/1986	EPO
WO 90/03432	04/1990	PCT
WO 90/01541	02/1990	PCT
WO 92/22646	12/1992	PCT
GB 2,213,831	08/1989	UK
WO 94/03585	02/1994	PCT

Other Art

Axelrod, H.R., "Embryonic Stem Cell Lines Derived from Blastocysts by a Simplified Technique," *Developmental Biology*, 101:225-228 (1984).

Bazer, F.W., *et al.*, "Fertilization, Cleavage and Implantation," in *Reproduction in Farm Animals*, 5th ed., ed. Hafez, E.S.E., Lea & Febiger, Philadelphia, PA (1987).

Bearden, J.H., *et al.*, "Gestation," *Applied Animal Reproduction*, pp. 85-98, Reston Publishing Company, Reston, VA (1980).

Bishop, Jerry E., "Sheep-Cloning Method Holds Promise Of Fast Introduction of Livestock Traits, News Article, 1996.

Bleck, G.T., *et al.*, "Single-Base Polymorphisms and DNA Sequence of the Porcine α-Lactalbumin 5′ Flanking Region," *J. Dairy Sci.*, (Suppl.1):946 (1994).

Bradley, A., *et al.*, "Formation of germline chimeras from embryo-derived teratocarcinoma cells lines," *Nature*, 309:255-256 (1984).

Brinster, *et al.*, "Targeted correction of a major histo-compatibility class II Eα gene by DNA microinjected into mouse eggs," *Proc. Natl. Acad. Sci.*, 86:7087-7091 (1989).

Capecchi, Mario R., "The new mouse genetics: Altering the genome by gene targeting," *Trends in Genetics*, 5(3):70-76 (1989).

Clark, A.J., *et al.*, "Germ line manipulation: applications in agriculture and biotechnology," *Transgenic Animals*, p. 250, Grosveld, *et al.*, eds., Academic Press Limited (1992).

Clark, *et al.*, "Expression of human anti-hemophilic factor IX in the milk of transgenic sheep," *Biotechnology*, Vol 7:487-492 (1989).

Cruz, Y.P., *et al.*, "Origin of embryonic and extraembryonic cell linages in mammalian embryos," in *Animal Application of Research in Mammalian Development*, eds. Pedersen, R.A., *et al.*, Cold Spring Harbor Laboratory Press, Plainview, NY (1991).

Doetschman, T., *et al.*, "Establishment of Hamster Blastocyst-Derived Embryonic Stem (ES) Cells," *Developmental Biology*, 127:224-227 (1988).

Ebert, K.M., *et al.*, "Changes in Domestic Livestock through Genetic Engineering," in *Current Communications 4 Cell & Molecular Biology, Animal Applications of Research in Mammalian Development*, ed. Pederson *et al.*, Cold Springs Harbor Laboratory Press, pp. 233-266 (1991).

Evans, M.J., *et al.*, "Establishment in culture of pluripotential cells from mouse embryos," *Nature*, 292:154-156 (1981).

Fajfar-Whetstone, C.F., *et al.*, "Sex Determination of Porcine Pre-Implantation Embryos via Y-Chromosome Specific DNA Sequence," *Anim. Biotech.*, 4:183-193 (1993).

Flake, A.W., *et al.*, "Transplantation of fetal hematopoietic stem cells in utero: the creation of hematopoietic chimeras," *Science*, vol. 233 (1986).

Frohman and Martin, "Cut, paste, and save: New approaches to altering specific genes in mice," *Cell*, 56:145-147 (1989).

Gossler, A., *et al.*, "Transgenesis by means of blastocyst-derived embryonic stem cell lines," *Proc. Natl. Acad. Sci. USA*, 83:9065-9069 (1986).

Hagen, D.R., *et al.*, *J. Anim. Sci.*, 69:1147-1150 (1991).

Handyside, A., *et al.*, "Towards the Isolation of Embryonal Stem Cell Lines from the Sheep," *Roux's Arch. Developmental Biology*, 196:185-190 (1987).

Hasty, *et al.*, "The length of homology required for gene targeting in embryonic stem cells," *Molecular and Cellular Biology*, 11(11):5586-5591 (1991).

Hogan, *et al.*, "Isolation of Pluripotential Stem Cell Lines," *Cold Spring Harbor Laboratory - Manipulating the Mouse Embryo: A Laboratory Manual*, Section E:205-218 (1986).

Hooper, M.C., *Teratocarcinomas and Embryonic Stem Cells: A Practical Approach*, ed. Robertson, E.J., IRL Press, Ltd., Oxford, UK, 51-70 (1987).

Jasin and Berg, "Homologous integration in mammalian cells without target gene selection," *Genes & Development*, 2:1353-1363 (1988).

Jeannotte, *et al.*, "Low level of Hox1.3 gene expression does not preclude the use of promoterless vectors to generate a targeted gene disruption," *Molecular and Cellular Biology*, 11(11):5578-5585.

Karg, H., "Manipulation of Lactation," in *Biotechnology for Livestock Production*, Plenum Press, New York and London, 19:181-206 (1989).

Karg, H., "Manipulation of Growth," in *Biotechnology for Livestock Production*, Plenum Press, New York and London, 18:159-180 (1989).

Kollias, G., *et al.*, "The study of gene regulation in transgenic mice," *Transgenic Animals*, p. 92, Grosveld, *et al.*, eds., Academic Press Limited (1992).

Lewin, H.A., *et al.*, "Mapping Genes for Resistance to Infectious Diseases in Animals," in *Gene-Mapping Techniques and Applications*, Marcel Dekker, Inc., 13:283-304 (1991).

Mansour, *et al.*, "Disruption of the proto-oncogene int-2 in mouse embryo-derived stem cells: A general strategy for targeting mutations to non-selectable genes," *Nature*, 336:348-352.

Martin, G.R., "Teratocarcinomas and Mammalian Embryogenesis," *Science*, 209:768-776 (1980).

Martin, G.R., "Isolation of a Pluripotent Cell Line from Early Mouse Embryos Cultured in Medium Conditioned by Teratocarcinoma Stem Cells," *Proc. Natl. Acad. Sci. USA*, 78(12):7634-7638 (1981).

Martin, P., *et al.*, "Improvement of milk protein quality by gene technology," *Livestock Production Science*, 35:95-115 (1993).

McLaren, A., *et al.*, *Nature*, 224, pp. 238-240 (1969).

Mintz, B., *Science*, 148, 1232-3 (1965).

Morgenstern and Land, *Nucleic Acids Res.*, 18:3587-3596 (1990).

Mortensen, *et al.*, "Production of homozygous mutant ES cells with a single targeting construct," *Molecular and Cellular Biology*, 12(5):2391-2395 (1992).

Nichols, J., *et al.*, "Establishment of germ-line-competent embryonic stem (ES) cells using differentiation inhibiting activity," *Development*, 110:1341-1348 (1990).

Notarianni, E., *et al.*, "Maintenance and differentiation in culture of pluripotential embryonic cell lines from pig blastocysts," *J. Reprod. Fert., Suppl.* 41:51-56 (1990).

Papaioannou, V.E., *et al.*, "Growth and differentiation of an embryonal carcinoma cell line (C145b)," *J. Embryol. Exp. Morph.*, 54, pp. 277-295 (1979).

Phillips, R.W., *et al.*, Models, pp. 437-440 in *Swine in Biomedical Research*, ed. Tumbleson, M.E., Vol. 1 (Plenum Press, New York), (1986).

Piedrahita, J.A., *et al.*, "Influence of Feeder Layer Type on the Efficiency of Isolation of Porcine Embryo-Derived Cell Lines", *Theriogenology*, 34(5):865-877 (1990).

Piedrahita, J.A., *et al.*, "On the Isolation of Embryonic Stem Cells: Comparative Behavior of Murine, Porcine and Ovine Embryos," *Theriogenology*, 34(5):879-901 (1990).

Polge, C., "Embryo transplantation and preservation," pp. 277-291 in *Control of Pig Reproduction*, Cole, D.J.A., *et al.*, eds., Butterworth Scientific, London (1982).

Robertson, E., *et al.*, "Germ-line transmission of genes introduced into cultured pluripotential cells by retroviral vector," *Nature*, 323:445-448 (1986).

Robertson, E.J., "Pluripotential stem cell lines as a route into the mouse germ line," *Trends Genet.*, 2:9-13 (1987).

Robertson, E.J., "Embryo-derived Stem Cell Lines," *Teratocarcinomas and Embryonic Stem Cells: A Practical Approach*, pp. 71-122, ed. Robertson, E.J., IRL Press (1987).

Rohrer, G.A., Alexander, L.J., Keele, J.W., Smith, T.P., Beattie, C.W., "A Microsatellite Linkage Map of the Porcine Genome," *Genetics*, 136:231-245 (1994).

Rossant, J., *et al.*, "The developmental potential of a euploid male teratocarcinoma cell line after blastocyst injection," *J. Embryol. Exp. Morph.*, 70:99-112 (1982).

Rossant, J., *et al.*, "The relationship between embryonic, embryonal carcinoma and embryo-derived stem cells," *Cell Differentiation*, 15:155-161 (1984).

Rudnicki, M.A., *et al.*, "Teratocarcinomas and Embryonic Stem Cells: A Practical Approach," *Methods and Induction of Differentiation in Embryonal Carcinoma Cell Lines*, pp. 19-49, ed. Robertson, IRL Press Ltd., Oxford, England (1987).

Schook, L.B., *et al.*, "Mapping Genes for Growth and Development," 4:75-92, in *Growth of the Pig*, ed. Hollis, CAB International, Wallingford, UK (1993).

Sims, M.M., *et al.*, "Production of Fetuses from Totipotent Cultured Bovine Inner Cell Mass Cells," *Theriogeneology*, 39:313 (1993).

Smith, A.G., *et al.*, "Buffalo Rat Liver Cells Produce a Diffusible Activity which Inhibits the Differentiation of Murine Embryonal Carcinomas and Embryonic Stem Cells," *Dev. Biol.*, 121:9 (1987).

Stevens, L.C., "The development of transplantable terato-carcinomas from intratesticular grafts of pre- and post-implantation mouse embryos," *Dev. Biol.*, 21, 364-382 (1970).

Strojek, R.M., *et al.*, "A Method for Cultivating Morphologically Undifferentiated Embryonic Stem Cells from Porcine Blastocysts," *Theriogenology*, 33(4):901-913 (1990).

Talbot, N.C., *et al.*, "Alkaline phosphatase staining of pig and sheep epiblast cells in culture," *Molecular Reproduction and Development*, 36:139-147 (1993).

Thomas, *et al.*, "High-fidelity gene targeting in embryonic stem cells by using sequence replacement vectors," *Molecular and Cellular Biology*, 12(7):2919-2923 (1992).

Thomas, K.R., *et al.*, "Site-Directed Mutagenesis by Gene Targeting in Mouse Embryo-Derived Stem Cells," *Cell*, 51:503-512 (1987).

Wall, R.J., *et al.*, "High-level synthesis of a heterologous milk protein in the mammary glands of transgenic swine," *Proc. Natl. Acad. Sci. USA*, 88, 1696-1700 (1991).

Ware, C.B., *et al.*, "Development of embryonic stem cell lines from farm animals," *Biology of Reproduction*, supplement, Vol. 38 (1988).

Webel, S.K., *et al.*, "Synchronous and asynchronous transfer of embryos in the pig," *J. Animal Science*, 30:565-568 (1970).

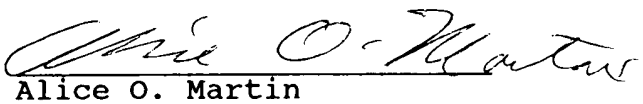
Wobus, A.M., *et al.*, "Characterization of a Pluripotent Stem Cell Line Derived from a Mouse Embryo," *Exp. Cell Res.*, 152:212-219 (1984).

Wurst, W., *et al.*, "Production of targeted embryonic stem cell clones," *Gene Targeting A Practical Approach*, p. 33, Joyner, A.L., ed., IRL Press (1993).

Yates, *et al.*, *Nature*, 313:811-815 (1985).

Respectfully submitted,

Date: May 31, 1996



Alice O. Martin
Registration No. 35,601
Attorney for Applicant

BRINKS HOFER GILSON & LIONE
P.O. BOX 10395
CHICAGO, ILLINOIS 60610
(312) 321-4200